

L Number	Hits	Search Text	DB	Time stamp
1	14	Ruvkun NEAR Gary	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/08/16 13:30
3	435	AFX OR FKHR	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/08/16 14:24
5	25	DAF-16 AND ELEGANS	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/08/16 14:19
4	10	DAF-16 AND (AFX OR FKHR)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/08/16 14:19
2	27	DAF-16	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/08/16 14:21
7	43	(AFX OR FKHR) AND ((glucose ADJ tolerance) OR atherosclerosis OR obesity)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/08/16 14:26
8	14	(US-6319708-\$ or US-6627746-\$ or US-6225120-\$).did. or (US-20010016332-\$ or US-20030082597-\$ or US-20030096957-\$ or US-20010029617-\$ or US-20020037585-\$ or US-20030036079-\$ or US-20030190312-\$ or US-20030181364-\$).did. or (WO-9851351-\$ or WO-9630053-\$).did. or (WO-200118549-\$).did.	USPAT; US-PGPUB; EPO; DERWENT	2004/08/16 14:29
-	4623	ELEGANS	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/11/13 22:12

=> d his

(FILE 'HOME' ENTERED AT 14:31:20 ON 16 AUG 2004)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
AT 14:31:35 ON 16 AUG 2004

L1 387 S DAF-16
L2 1357 S AFX OR FKHR
L3 17014 S C. ELEGAN?
L4 31 S L2 (L) L3
L5 12 DUP REM L4 (19 DUPLICATES REMOVED)
L6 88 S L1 (L) L2
L7 34 DUP REM L6 (54 DUPLICATES REMOVED)
L8 1 S L7 AND PY<=1997
L9 331031 S (GLUCOSE TOLERANCE) OR OBESITY OR ATHEROSCLEROSIS
L10 4 S L9 (L) L2
L11 3 DUP REM L10 (1 DUPLICATE REMOVED)
L12 9 S L9 (L) L1
L13 5 DUP REM L12 (4 DUPLICATES REMOVED)
E RUVKUN G?/AU
L14 108 S E4
L15 5 S L14 AND L1 AND L2
L16 5 DUP REM L15 (0 DUPLICATES REMOVED)

=> d an ti so au ab pi l16 5

L16 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:702845 CAPLUS

DN 128:20747

TI The Fork head transcription factor **DAF-16** transduces
insulin-like metabolic and longevity signals in *C. elegans*

SO Nature (London) (1997), 389(6654), 994-999

CODEN: NATUAS; ISSN: 0028-0836

AU Ogg, Scott; Paradis, Suzanne; Gottlieb, Shoshanna; Patterson, Garth I.;
Lee, Linda; Tissenbaum, Heidi A.; **Ruvkun, Gary**

AB In mammals, insulin signaling regulates glucose transport together with
the expression and activity of various metabolic enzymes. In the nematode
Caenorhabditis elegans, a related pathway regulates metabolism, development
and longevity. Wild-type animals enter the developmentally arrested dauer
stage in response to high levels of a secreted pheromone, accumulating
large amts. of fat in their intestines and hypodermis. Mutants in **DAF-2**
(a homolog of the mammalian insulin receptor) and **AGE-1** (a homolog of the
catalytic subunit of mammalian phosphatidylinositol 3-OH kinase) arrest
development at the dauer stage. Moreover, animals bearing weak or
temperature-sensitive mutations in **daf-2** and **age-1** can develop reproductively,
but nevertheless show increased energy storage and longevity. Null
mutations in **daf-16** suppress the effects of mutations
in **daf-2** or **age-1**; lack of **daf-16** bypasses the need
for this insulin receptor-like signaling pathway. **DAF-16**
is widely expressed and encodes three members of the Fork head
family of transcription factors. The **DAF-2** pathway acts synergistically
with the pathway activated by a nematode TGF- β -type signal, **DAF-7**,
suggesting that **DAF-16** cooperates with nematode SMAD
proteins in regulating the transcription of key metabolic and
developmental control genes. The probable human orthologs of **DAF-16**,
FKHR and **AFX**, may also act downstream
of insulin signaling and cooperate with TGF- β effectors in mediating
metabolic regulation. These genes may be dysregulated in diabetes.

=>

=> d his

(FILE 'HOME' ENTERED AT 14:31:20 ON 16 AUG 2004)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
AT 14:31:35 ON 16 AUG 2004

L1 387 S DAF-16
L2 1357 S AFX OR FKHR
L3 17014 S C. ELEGAN?
L4 31 S L2 (L) L3
L5 12 DUP REM L4 (19 DUPLICATES REMOVED)
L6 88 S L1 (L) L2
L7 34 DUP REM L6 (54 DUPLICATES REMOVED)
L8 1 S L7 AND PY<=1997
L9 331031 S (GLUCOSE TOLERANCE) OR OBESITY OR ATHEROSCLEROSIS
L10 4 S L9 (L) L2
L11 3 DUP REM L10 (1 DUPLICATE REMOVED)
L12 9 S L9 (L) L1
L13 5 DUP REM L12 (4 DUPLICATES REMOVED)

=> d an ti so au ab pi l13 5 2

L13 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:761816 CAPLUS
DN 130:29188
TI Therapeutic and diagnostic tools for impaired glucose tolerance conditions
based on the dauer polypeptides and genes of Caenorhabditis elegans
SO PCT Int. Appl., 202 pp.
CODEN: PIXXD2
IN Ruvkun, Gary; Kimura, Koutarou; Patterson, Garth; Ogg, Scott; Paradis,
Suzanne; Tissenbaum, Heidi; Morris, Jason; Kowek, Allison; Pierce, Sarah
AB Disclosed herein are novel genes and methods for the screening of
therapeutics useful for treating impaired **glucose**
tolerance conditions, as well as diagnostics and therapeutic
comps. for identifying or treating such conditions. The Caenorhabditis
elegans metabolic regulatory genes daf-2 and age-1 encode homologs of the
mammalian insulin receptor/phosphoinositide 3-kinase signaling pathway
proteins, resp. In addition, the **DAF-16** forkhead protein
represents the major transcriptional output of this insulin signaling
pathway. Dysregulation of the **DAF-16** transcription
factor in the absence of insulin signaling leads to metabolic defects;
inactivation of **DAF-16** reverses the metabolic defects
caused by lack of insulin signaling in C. elegans. Finally, the C.
elegans daf-7, da-1, daf-4, daf-8, daf-14, and daf-3 genes encode
neuroendocrine/target tissue transforming growth factor- β type signal
transduction mols. that genetically interact with the insulin signaling
pathway. Metabolic defects cause by lack of neuroendocrine TGF- β
signals can be reversed by inactivation of the DAF-3 transcription factor.
The C. elegans daf genes are excellent candidate genes and proteins for
human disease associated with glucose intolerance, e.g., diabetes,
obesity, and **atherosclerosis**. The human homologs of
these daf genes and proteins mediate insulin signaling in normal people
and may be defective or mis-regulated in diabetics. Moreover, there are
at least 2 classes of type II diabetics: those with defects in the
TGF- β signaling genes, and those with defects in insulin signaling
genes. Exemplary sequences and functional characteristics are provided
for the C. elegans daf homologs of the human genes: daf-2, daf-3 (3
differentially spliced isoforms), **daf-16** (2
differentially spliced isoforms), age-1, and pdk-1 (two spliced isoforms).
PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 9851351 A1 19981119 WO 1998-US10080 19980515
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,

	CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 6225120	B1	20010501	US 1997-857076	19970515
AU 9874941	A1	19981208	AU 1998-74941	19980515
AU 752962	B2	20021003		
EP 1019092	A1	20000719	EP 1998-922382	19980515
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2002511747	T2	20020416	JP 1998-549639	19980515
US 2001029617	A1	20011011	US 1998-205658	19981203
US 2002037585	A1	20020328	US 2001-844353	20010427
US 2003181364	A1	20030925	US 2001-963693	20010925

L13 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:384548 CAPLUS

DN 133:39116

TI Genes and polypeptides involved in insulin signaling pathways for glucose tolerance, obesity, and longevity and their uses as therapeutic and diagnostic tools

SO PCT Int. Appl., 402 pp.

CODEN: PIXXD2

IN Ruvkun, Gary; Ogg, Scott

AB Disclosed herein are novel genes and methods for the screening of therapeutics useful for treating impaired **glucose tolerance** conditions, as well as diagnostics and therapeutic compns. for identifying or treating such conditions. The *Caenorhabditis elegans* metabolic regulatory genes *daf-2* and *age-1* encode homologs of the mammalian insulin receptor/phosphoinositol 3-kinase signaling pathway proteins, resp. Also, the *C. elegans* PKB kinase and AKT kinase act downstream of these genes, as their mammalian homologs act downstream of insulin signaling. The *C. elegans* PTEN lipid phosphatase homolog, DAF-18, acts upstream of AKT in this signaling pathway. Further, the **DAF-16** forkhead protein represents the major transcriptional output of this insulin signaling pathway. Addnl. evidence indicates that the **DAF-16**, DAF-3, DAF-8, and DAF-14 transcriptional outputs of converging signaling pathways regulate metabolism. The congruence between the *C. elegans* and mammalian insulin signaling pathways strongly supports the contention that new genes identified in the *C. elegans* pathway also act in mammalian insulin signaling. Exemplary sequences and functional characteristics of the *C. elegans* *daf* genes and their human homologs are provided.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000033068	A1	20000608	WO 1999-US28529	19991202
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 2001029617	A1	20011011	US 1998-205658	19981203
EP 1163515	A1	20011219	EP 1999-960641	19991202
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

=>

L5 ANSWER 8 OF 12 MEDLINE on STN DUPLICATE 6
 AN 2000484170 MEDLINE
 TI DAF-16 recruits the CREB-binding protein coactivator complex to the insulin-like growth factor binding protein 1 promoter in HepG2 cells.
 SO Proceedings of the National Academy of Sciences of the United States of America, (2000 Sep 12) 97 (19) 10412-7.
 Journal code: 7505876. ISSN: 0027-8424.
 AU Nasrin N; Ogg S; Cahill C M; Biggs W; Nui S; Dore J; Calvo D; Shi Y; Ruvkun G; Alexander-Bridges M C
 AB Insulin negatively regulates expression of the insulin-like growth factor binding protein 1 (IGFBP-1) gene by means of an insulin-responsive element (IRE) that also contributes to glucocorticoid stimulation of this gene. We find that the *Caenorhabditis elegans* protein DAF-16 binds the IGFBP-1 small middle dotIRE with specificity similar to that of the forkhead (FKH) factor(s) that act both to enhance glucocorticoid responsiveness and to mediate the negative effect of insulin at this site. In HepG2 cells, DAF-16 and its mammalian homologs, **FKHR**, **FKHRL1**, and **AFX**, activate transcription through the IGFBP-1.IRE; this effect is inhibited by the viral oncoprotein E1A, but not by mutants of E1A that fail to interact with the coactivator p300/CREB-binding protein (CBP). We show that DAF-16 and **FKHR** can interact with both the KIX and E1A/SRC interaction domains of p300/CBP, as well as the steroid receptor coactivator (SRC). A C-terminal deletion mutant of DAF-16 that is nonfunctional in *C. elegans* fails to bind the KIX domain of CBP, fails to activate transcription through the IGFBP-1.IRE, and inhibits activation of the IGFBP-1 promoter by glucocorticoids. Thus, the interaction of DAF-16 homologs with the KIX domain of CBP is essential to basal and glucocorticoid-stimulated transactivation. Although **AFX** interacts with the KIX domain of CBP, it does not interact with SRC and does not respond to glucocorticoids or insulin. Thus, we conclude that DAF-16 and **FKHR** act as accessory factors to the glucocorticoid response, by recruiting the p300/CBP/SRC coactivator complex to an FKH factor site in the IGFBP-1 promoter, which allows the cell to integrate the effects of glucocorticoids and insulin on genes that carry this site.

L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2000:384548 CAPLUS
 DN 133:39116
 TI Genes and polypeptides involved in insulin signaling pathways for glucose tolerance, obesity, and longevity and their uses as therapeutic and diagnostic tools
 SO PCT Int. Appl., 402 pp.
 CODEN: PIXXD2
 IN Ruvkun, Gary; Ogg, Scott
 AB Disclosed herein are novel genes and methods for the screening of therapeutics useful for treating impaired glucose tolerance conditions, as well as diagnostics and therapeutic compns. for identifying or treating such conditions. The *Caenorhabditis elegans* metabolic regulatory genes *daf-2* and *age-1* encode homologs of the mammalian insulin receptor/phosphoinositol 3-kinase signaling pathway proteins, resp. Also, the *C. elegans* PKB kinase and AKT kinase act downstream of these genes, as their mammalian homologs act downstream of insulin signaling. The *C. elegans* PTEN lipid phosphatase homolog, DAF-18, acts upstream of AKT in this signaling pathway. Further, the DAF-16 forkhead protein represents the major transcriptional output of this insulin signaling pathway. Addnl. evidence indicates that the DAF-16, DAF-3, DAF-8, and DAF-14 transcriptional outputs of converging signaling pathways regulate metabolism. The congruence between the *C. elegans* and mammalian insulin signaling pathways strongly supports the contention that new genes identified in the *C. elegans* pathway also act in mammalian insulin signaling. Exemplary sequences and functional characteristics of the *C. elegans* *daf* genes and their human homologs are provided.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000033068	A1	20000608	WO 1999-US28529	19991202
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001029617	A1	20011011	US 1998-205658	19981203
EP 1163515	A1	20011219	EP 1999-960641	19991202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				



Entrez PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Books

Search PubMed for [] Go Clear
Limits Preview/Index History Clipboard Details

About Entrez

Text Version

Entrez PubMed

Overview

Help | FAQ

Tutorial

New/Noteworthy

E-Utilities

PubMed Services

Journals Database

MeSH Database

Single Citation Matcher

Batch Citation Matcher

Clinical Queries

LinkOut

Cubby

Related Resources

Order Documents

NLM Gateway

TOXNET

Consumer Health

Clinical Alerts

ClinicalTrials.gov

PubMed Central

- The Clipboard will hold a maximum of 500 items.
- Clipboard items will be lost after eight hours of inactivity.

Display Summary Show: 20 Sort Send to Text
Items 1-10 of 10 One page.

1: [Ogg S, Paradis S, Gottlieb S, Patterson GI, Lee L, Tissenbaum HA, Ruvkun G.](#) Related Articles, Links



The Fork head transcription factor DAF-16 transduces insulin-like metabolic and longevity signals in *C. elegans*.

Nature. 1997 Oct 30;389(6654):994-9.

PMID: 9353126 [PubMed - indexed for MEDLINE]

2: [Lin K, Dorman JB, Rodan A, Kenyon C.](#) Related Articles, Links



daf-16: An HNF-3/forkhead family member that can function to double the life-span of *Caenorhabditis elegans*.

Science. 1997 Nov 14;278(5341):1319-22.

PMID: 9360933 [PubMed - indexed for MEDLINE]

3: [Lee SS, Kennedy S, Tolonen AC, Ruvkun G.](#) Related Articles, Links



DAF-16 target genes that control *C. elegans* life-span and metabolism.

Science. 2003 Apr 25;300(5619):644-7. Epub 2003 Apr 10.

PMID: 12690206 [PubMed - indexed for MEDLINE]

4: [Ookuma S, Fukuda M, Nishida E.](#) Related Articles, Links



Identification of a DAF-16 transcriptional target gene, *scl-1*, that regulates longevity and stress resistance in *Caenorhabditis elegans*.

Curr Biol. 2003 Mar 4;13(5):427-31.

PMID: 12620193 [PubMed - indexed for MEDLINE]

5: [Hsu AL, Murphy CT, Kenyon C.](#) Related Articles, Links



Regulation of aging and age-related disease by DAF-16 and heat-shock factor.

Science. 2003 May 16;300(5622):1142-5. Erratum in: Science. 2003 Jun 27;300(5628):2033.

PMID: 12750521 [PubMed - indexed for MEDLINE]

6: [Tissenbaum HA, Ruvkun G.](#) Related Articles, Links



An insulin-like signaling pathway affects both longevity and reproduction in *Caenorhabditis elegans*.

Genetics. 1998 Feb;148(2):703-17.

PMID: 9504918 [PubMed - indexed for MEDLINE]

7: [Lin K, Hsin H, Libina N, Kenyon C.](#) Related Articles, Links





Regulation of the *Caenorhabditis elegans* longevity protein DAF-16 by insulin/IGF-1 and germline signaling.


Nat Genet. 2001 Jun;28(2):139-45.


PMID: 11381260 [PubMed - indexed for MEDLINE]


8: [Yu H, Larsen PL.](#) Related Articles, Links

 DAF-16-dependent and independent expression targets of DAF-2 insulin receptor-like pathway in *Caenorhabditis elegans* include FKBP. [J Mol Biol.](#) 2001 Dec 14;314(5):1017-28.
PMID: 11743719 [PubMed - indexed for MEDLINE]

 **9:** [Murphy CT, McCarroll SA, Bargmann CI, Fraser A, Kamath RS, Ahringer J, Li H, Kenyon C.](#) [Related Articles, Links](#)

 Genes that act downstream of DAF-16 to influence the lifespan of *Caenorhabditis elegans*.
[Nature.](#) 2003 Jul 17;424(6946):277-83. Epub 2003 Jun 29.
PMID: 12845331 [PubMed - indexed for MEDLINE]

 **10:** [Lee RY, Hench J, Ruvkun G.](#) [Related Articles, Links](#)

 Regulation of *C. elegans* DAF-16 and its human ortholog FKHRL1 by the daf-2 insulin-like signaling pathway.
[Curr Biol.](#) 2001 Dec 11;11(24):1950-7.
PMID: 11747821 [PubMed - indexed for MEDLINE]

Display **Summary**  **Show:** **20**  **Sort**  **Send to** **Text** 

[Write to the Help Desk](#)
[NCBI](#) | [NLM](#) | [NIH](#)
[Department of Health & Human Services](#)
[Privacy Statement](#) | [Freedom of Information Act](#) | [Disclaimer](#)

Jul 27 2004 06:47:37